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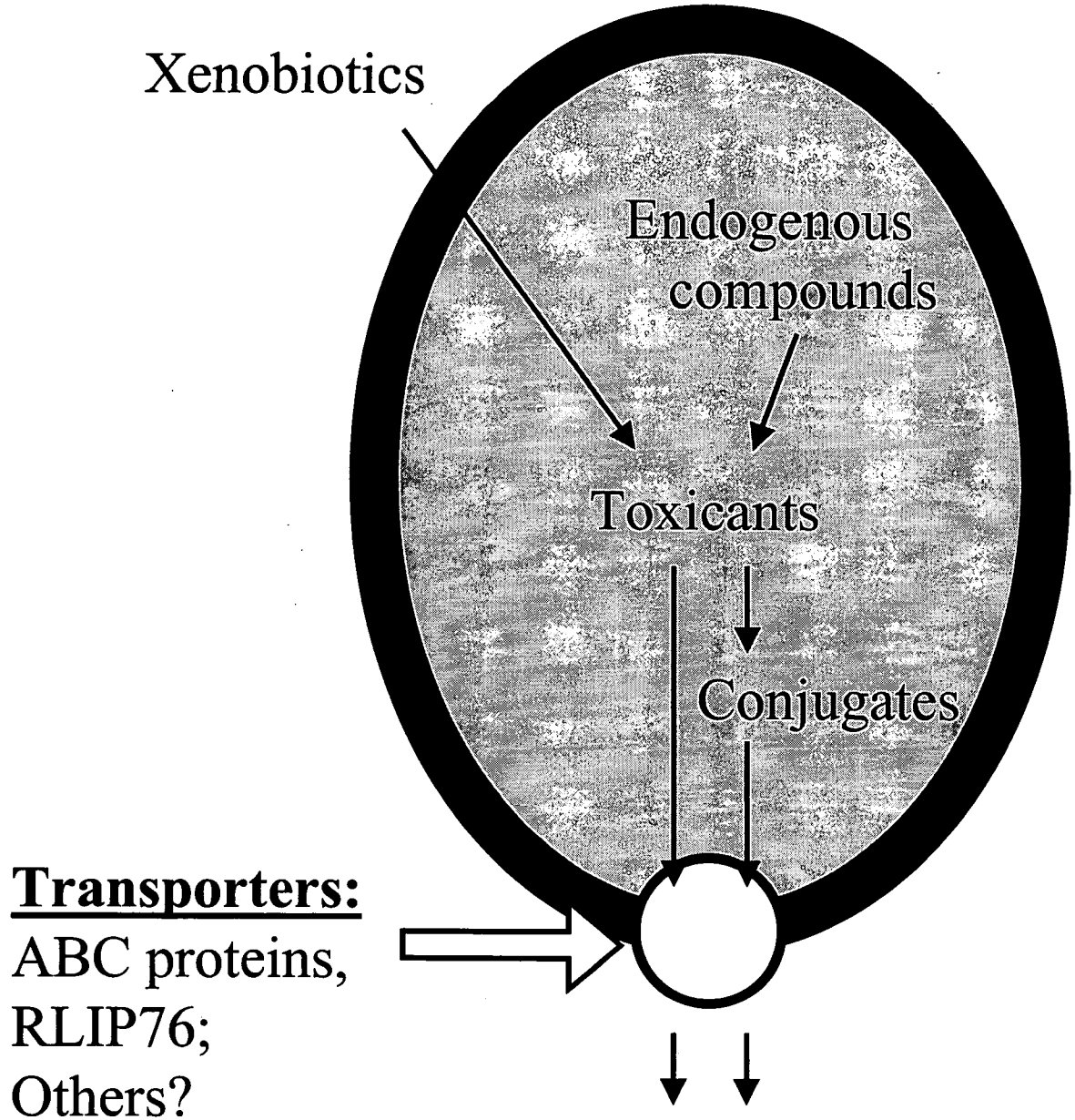
Fig. 1


Xenobiotics
Endogenous compounds
Toxicants
Conjugates
Transporters:
ABC proteins,
RLIP76;
Others?

RLIP76, A NOVEL TRANSPORTER OF XENOBIOTICS

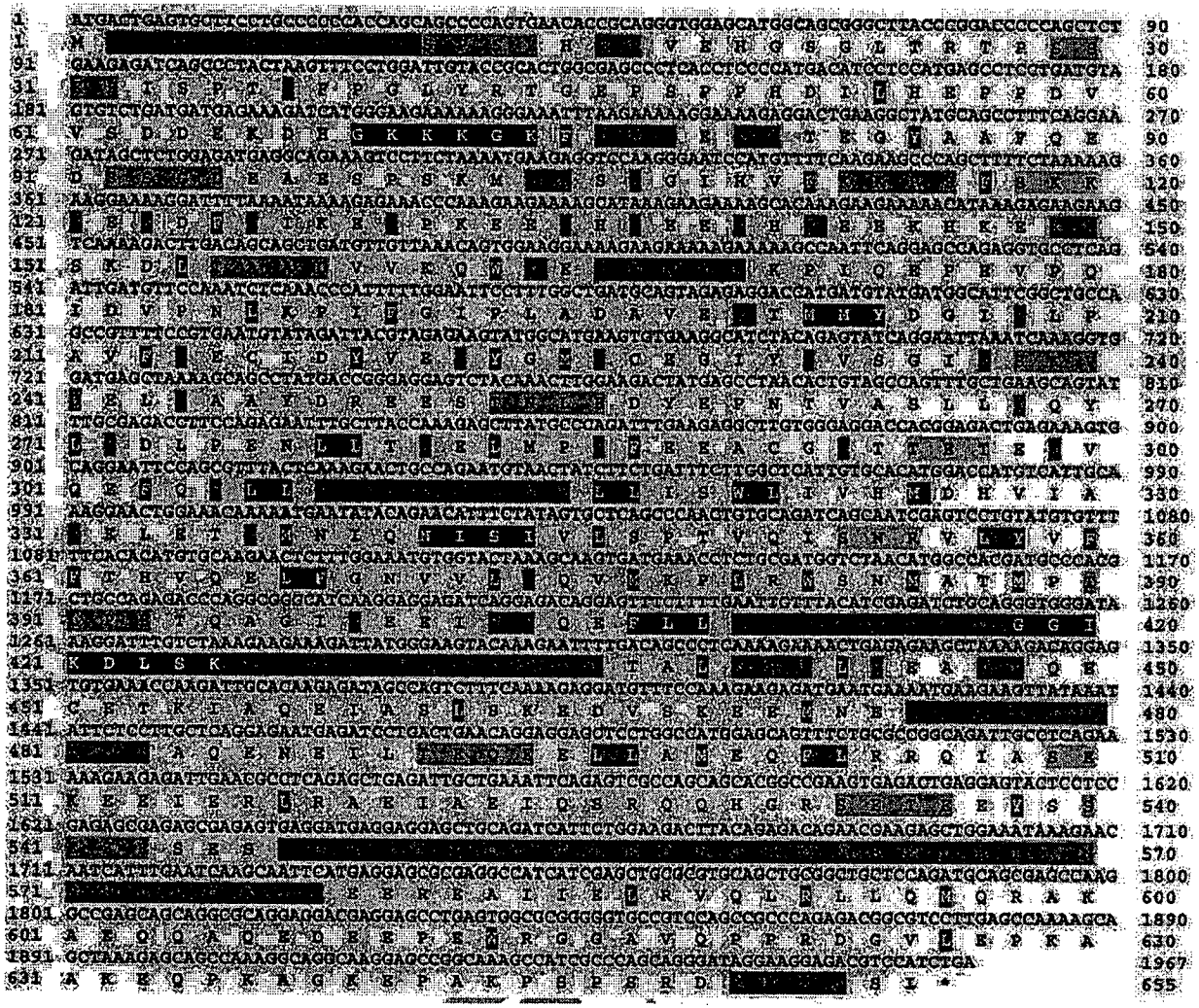


Fig. 2

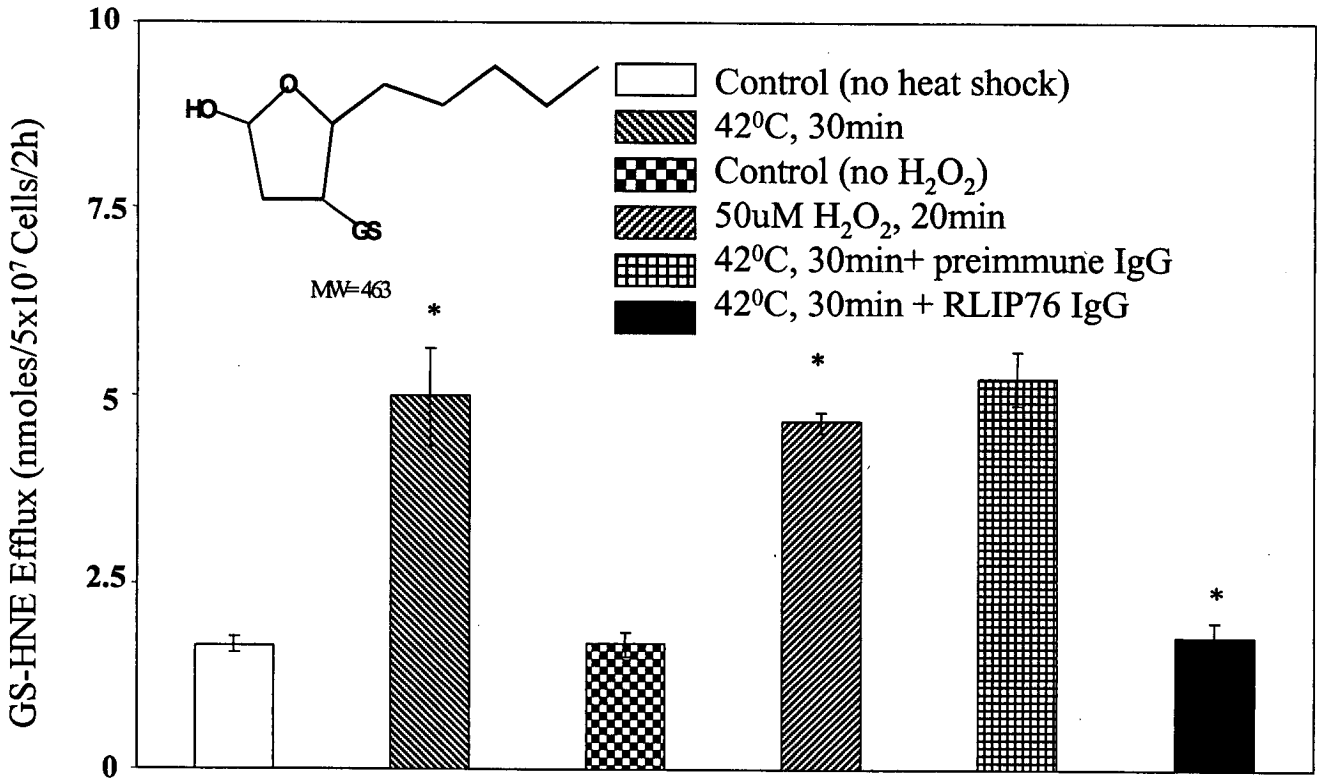

10
7.5
5
2.5
0
GS-HNE Efflux (nmoles/5x10⁷ Cells/2h)
HO
O
GS
MW=463
Control (no heat shock)
42⁰C, 30min
Control (no H2O2)
50uM H2O2, 20min
42⁰C, 30min+ preimmune IgG
42⁰C, 30min + RLIP76 IgG
*
*
*

Fig. 3

Fig.4A

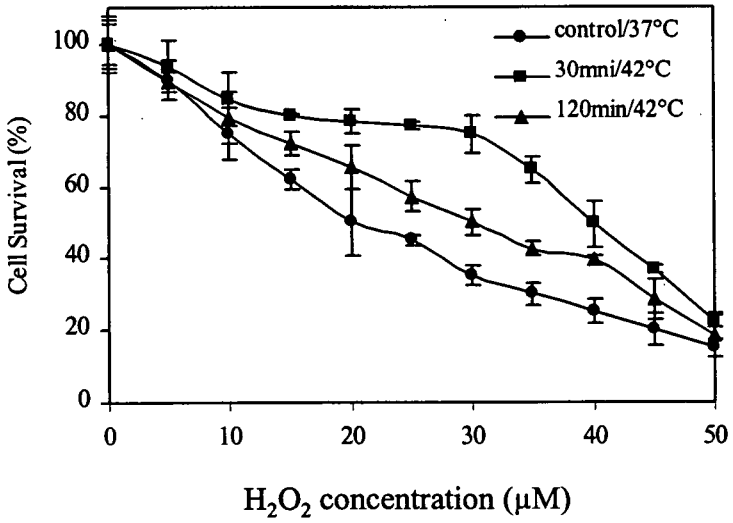

control/37°C
30mni/42°C
120min/42°C
Cell Survival (%)
100
80
60
40
20
0
0
10
20
30
40
50
H_2O_2 concentration (μM)

Fig.4B

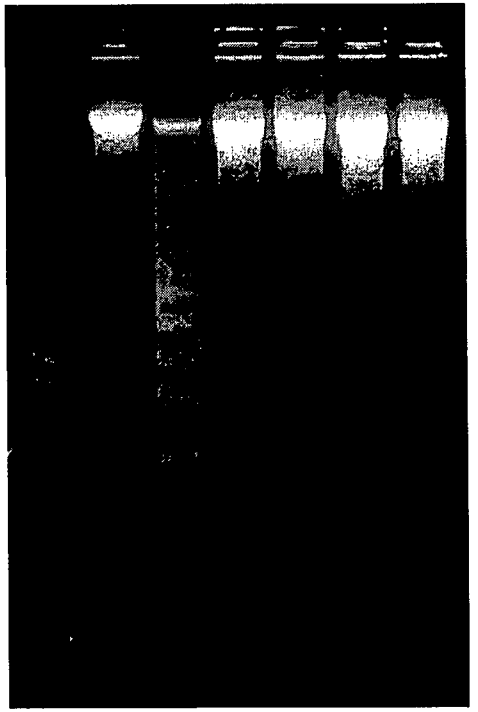
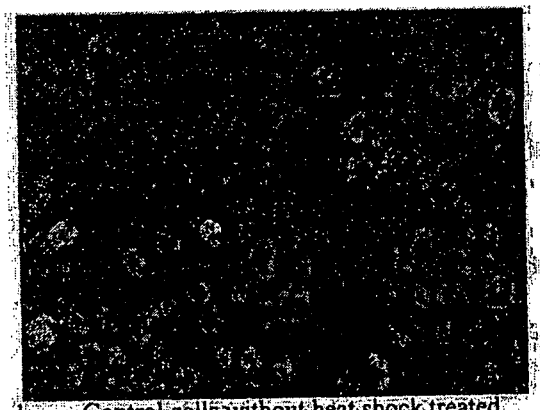
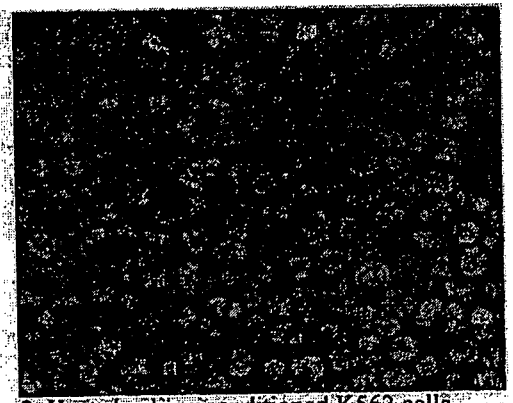

Markers
Control
H_2O_2 (100 μM, 2 h)
Heat shock pre-treatment
Heat shock pre-treatment + H_2O_2 (100 μM, 2 h)
H_2O_2 pre-treatment
H_2O_2 pre-treatment + H_2O_2 (100 μM, 2 h)

Fig. 5

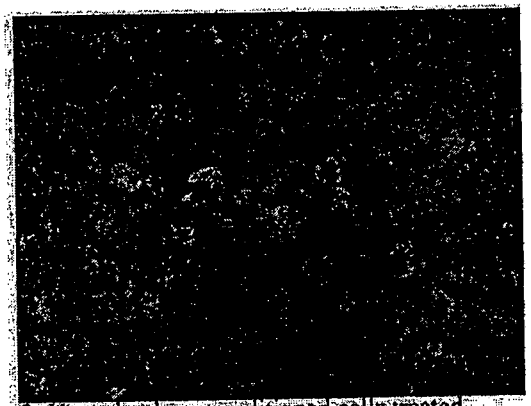
RLIP76, A NOVEL TRANSPORTER OF XENOBIOTICS



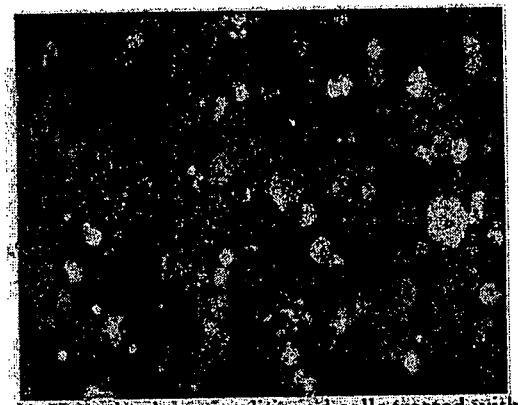
1. Control cells without heat shock treated with 4-HNE



2. Heat shock preconditioned K562 cells



3. Heat shock preconditioned cells treated with 4-HNE



4. Heat shock preconditioned cells treated with 4-HNE after coating with anti-RLIP76 IgG

Fig.6

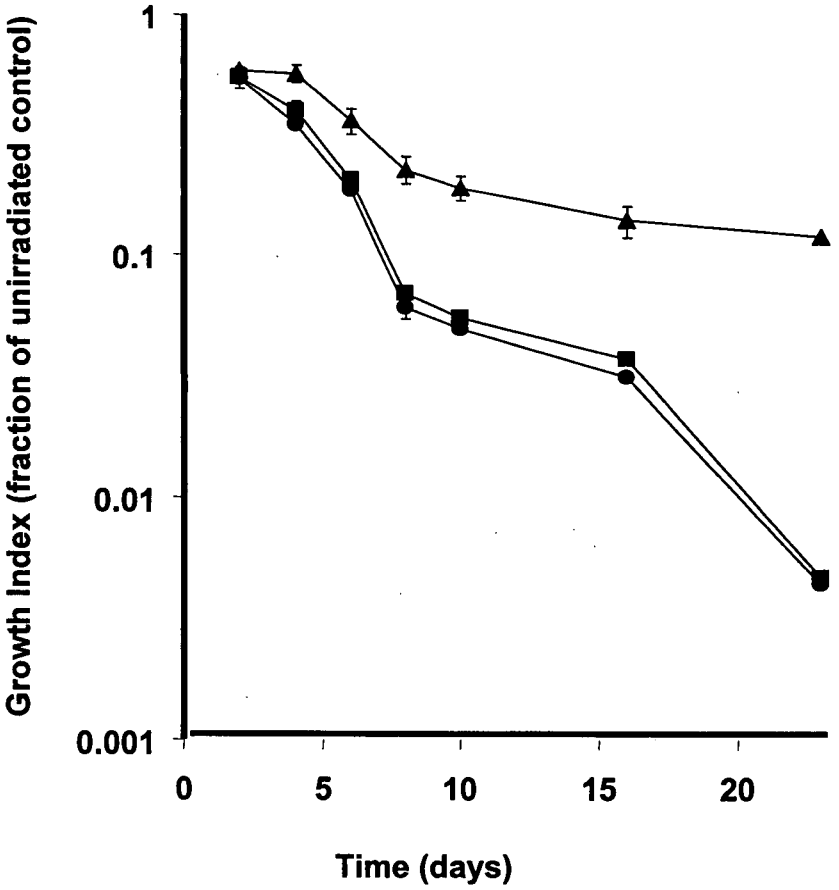

Growth Index (fraction of unirradiated control)
1
0.1
0.01
0.001
0
5
10
15
20
Time (days)

Fig. 7

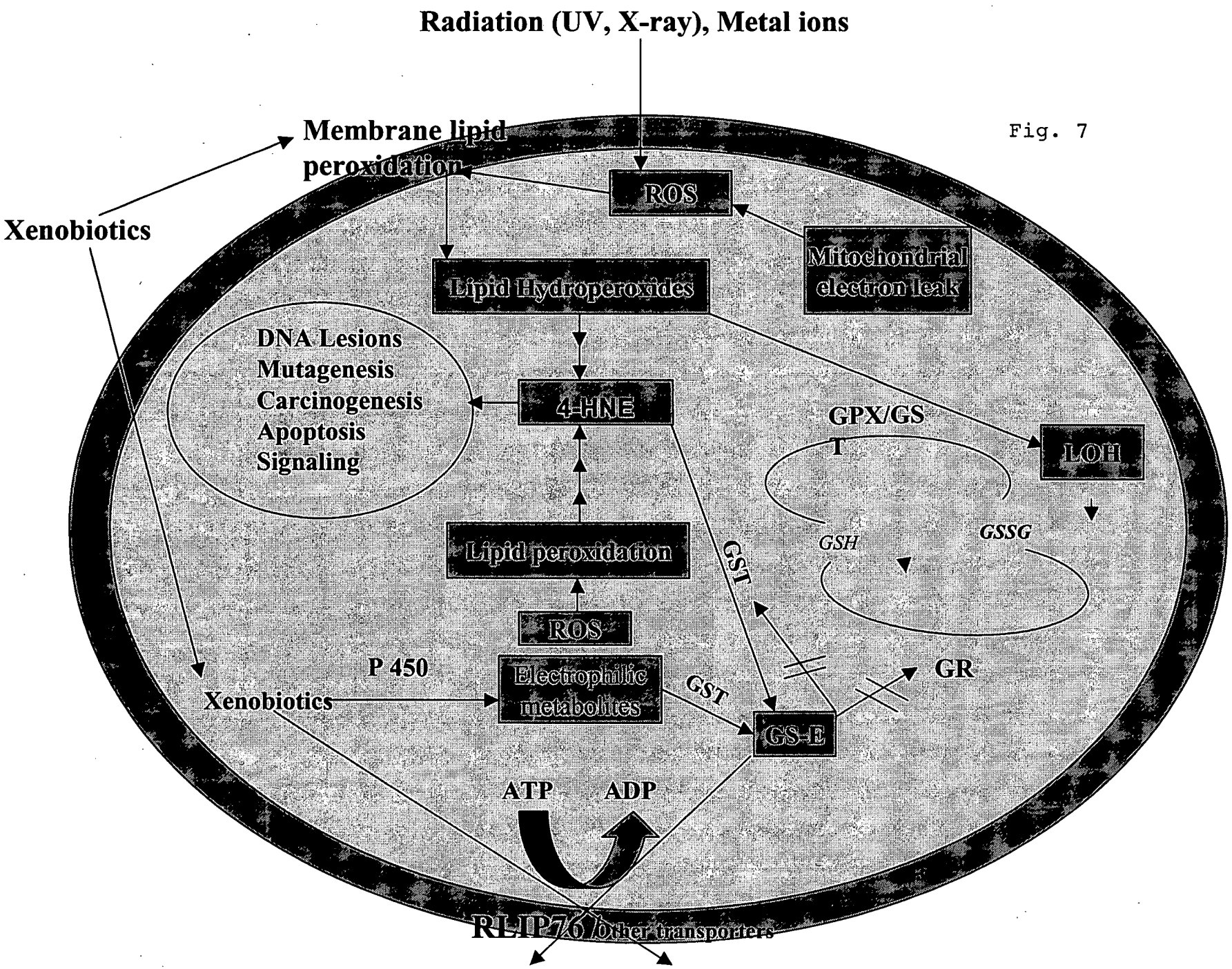

Radiation (UV, X-ray), Metal ions
Membrane lipid peroxidation
Xenobiotics
ROS
Mitochondrial electron leak
Lipid Hydroperoxides
DNA Lesions
Mutagenesis
Carcinogenesis
Apoptosis
Signaling
4-HNE
GPX/GS T
LOH
GSH
GSSG
Lipid peroxidation
GST
ROS
P 450
Xenobiotics
Electrophilic metabolites
GST
GR
GS-E
ATP
ADP
RLIP76
other transporters

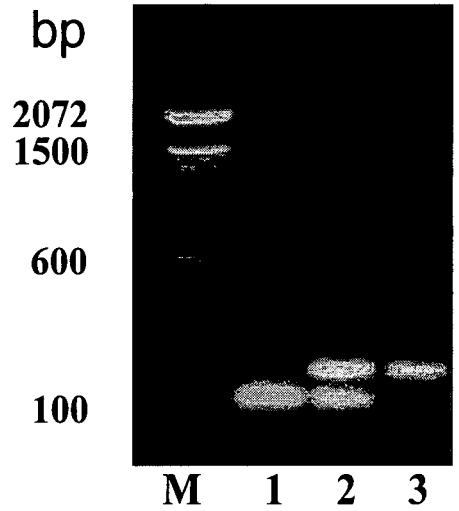
Fig. 8

A. **Sequence around the insertion site**

5'TTTGTTAAATTTTCTA**TCTTCTGCTCACTCGTCCCT**TAACAGTTGCTGTTAATAAGGGGGACAGTATACACTAGACCCTGTTACAGTGCAGTTAT
AGAATGTCACATTTTTAAAGTTGACTCTGCCTGOAGGGCTTGCTTTAGGTA-**insertion site**-TGCTATTTTACTTTGCCAAGATG**CTGGAAGCTGAGT-GGGAAAC**AAGTTGTAGAGCTCAGTGGGGGGGAGGCCAATGAGAAGTTTGCTTGTTAGACTAAGCCCCGGCCATAGGGGAAGGTAAGTCAAAGAT
TAAGGCTGATGATTTATAAGGAAAAATCCAAAGGAGTCAAGTGTGGGTTAAGTACACCTTAATGATGTTAGTAGGTTTAAGAGGATTAATTATGTA
ACAGCTCAGTTAGGTAATAATTGG 3'

B. **LTR-primer:**5' – AAATGGCGTTACTTAAGCTAGCTTGC – 3'

C.



D.

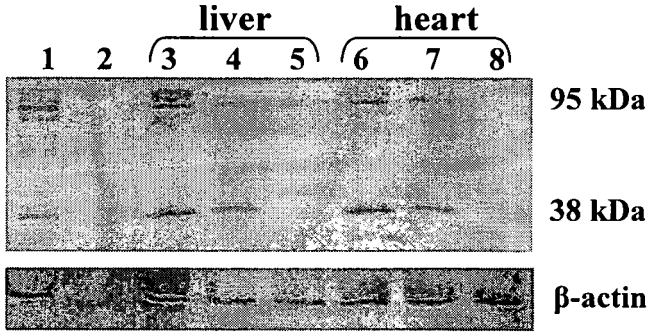


Fig. 9

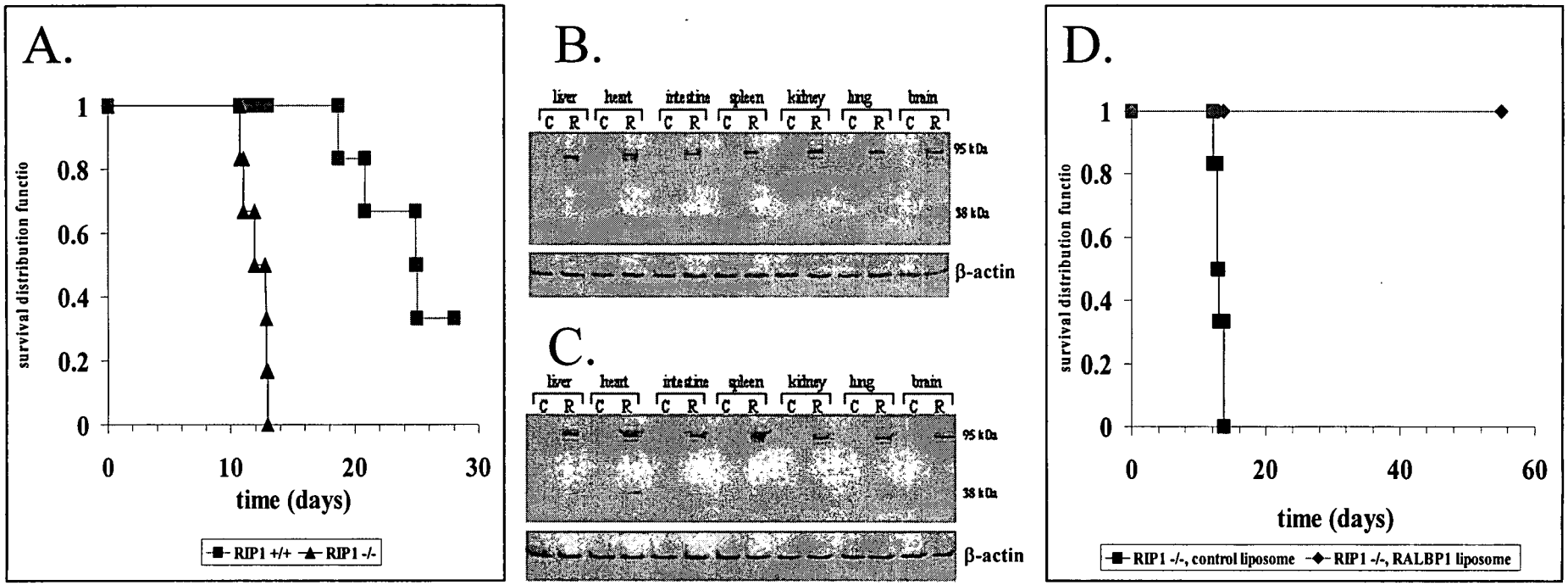
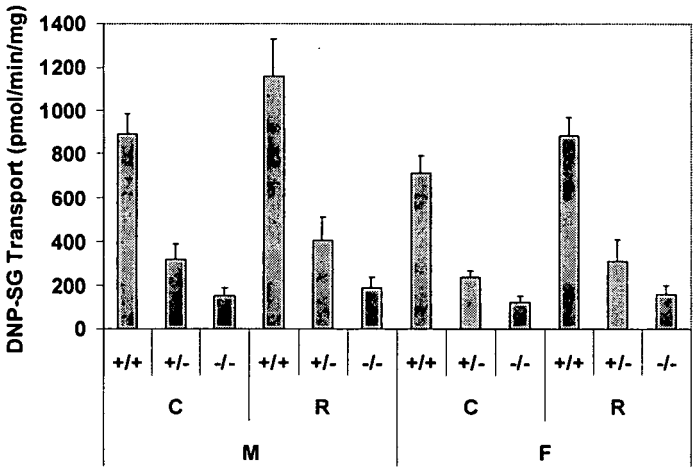
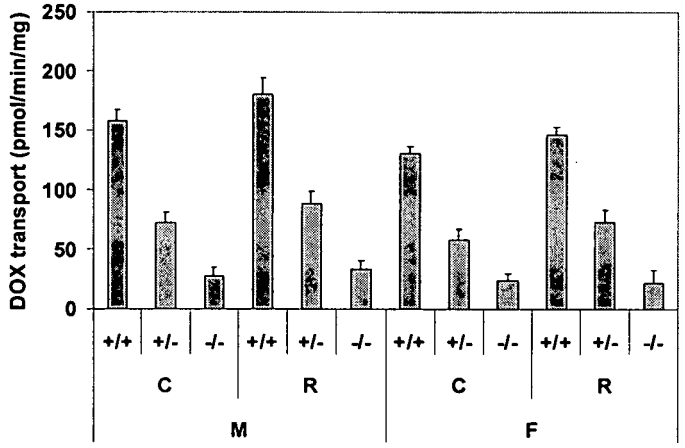

A.
survival distribution functio
1
0.8
0.6
0.4
0.2
0
0
10
20
30
time (days)
RIP1 +/+
RIP1 -/-
B.
liver
heart
intestine
spleen
kidney
lung
brain
C R
95 kDa
38 kDa
β-actin
C.
liver
heart
intestine
spleen
kidney
lung
brain
C R
95 kDa
38 kDa
β-actin
D.
survival distribution functio
1
0.8
0.6
0.4
0.2
0
0
20
40
60
time (days)
RIP1 -/-, control liposome
RIP1 -/-, RALBP1 liposome

Fig. 10





	Unirratiated				Irratiated			
	+/- (Fold)		-/- (Fold)		+/- (Fold)		-/- (Fold)	
	M	F	M	F	M	F	M	F
DNP-SG Transport*	↓ (0.35)	↓ (0.33)	↓ (0.19) **↓ (0.54)**	↓ (0.18) **↓ (0.53)**	↓ (0.45)	↓ (0.44)	↓ (0.17) **↓ (0.49)**	↓ (0.21) **↓ (0.63)**
DOX Transport*	↓ (0.49)	↓ (0.45)	↓ (0.15) **↓ (0.31)**	↓ (0.18) **↓ (0.41)**	↓ (0.6)	↓ (0.55)	↓ (0.23) **↓ (0.47)**	↓ (0.21) **↓ (0.47)**

FIG. 11

Organ	LOOH				TBARS				GSH				GGCS			
	+/-		-/-		+/-		-/-		+/-		-/-		+/-		-/-	
	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F
Liver	-	-	↓ (0.77) **↓ (0.79)**	-	↓ (0.79)	-	↓ (0.47) **↓ (0.60)**	↓ (0.63) **↓ (0.71)**	-	↓ (0.86)	↓ (0.76) **↓ (0.77)**	↓ (0.86) -	↑ (3.63)	-	↑ (5.25) **↑ (1.45)**	↑ (1.16) -
Lung	↑ (1.32)	↑ (1.23)	↑ (1.62) **↑ (1.23)**	↑ (1.96) **↑ (1.59)**	-	-	↑ (1.17) -	↑ (1.19) -	↑ (1.19)	↑ (1.07)	↑ (1.41) -	- -	-	-	- -	- -
Kidney	↑ (1.20)	↑ (1.18)	↑ (1.43) **↑ (1.19)**	↑ (1.53) **↑ (1.29)**	-	-	- **↑ (1.06)**	- -	-	-	- **↑ (1.19)**	↑ (1.11) -	↓ (0.65)	-	↓ (0.57) **↓ (0.85)**	↓ (0.73) **↓ (0.80)**
Heart	↑ (1.47)	↑ (1.75)	↑ (3.12) **↑ (2.12)**	↑ (2.56) **↑ (1.46)**	↑ (1.26)	-	↑ (1.93) **↑ (1.54)**	↑ (1.54) **↑ (1.35)**	↑ (1.55)	↑ (1.77)	↑ (1.69) **↑ (1.09)**	↑ (1.88) -	↓ (0.68)	↓ (0.70)	↓ (0.60) **↓ (0.88)**	↓ (0.54) **↓ (0.78)**
Brain	-	↑ (1.16)	↑ (1.32) **↑ (1.25)**	↑ (1.28) -	↑ (1.16)	↑ (1.16)	↑ (1.61) **↑ (1.38)**	↑ (1.46) **↑ (1.26)**	↑ (1.45)	↑ (1.31)	↑ (1.68) -	↑ (1.41) -	-	↑ (1.15)	- -	↓ (0.77) **↓ (0.67)**
Intestine	↑ (1.56)	↑ (1.55)	↑ (2.13) **↑ (1.48)**	↑ (2.40) **↑ (1.50)**	↑ (1.60)	↑ (1.58)	↑ (2.95) **↑ (1.84)**	↑ (2.98) **↑ (1.40)**	↑ (2.61)	↑ (2.48)	↑ (2.91) -	↑ (2.57) -	↓ (0.72)	↓ (0.79)	↓ (0.58) **↓ (0.80)**	↓ (0.70) -
Spleen	↑ (1.63)	↑ (1.52)	↑ (2.99) **↑ (1.83)**	↑ (3.39) **↑ (2.23)**	↑ (1.46)	↑ (1.47)	↑ (2.54) **↑ (1.73)**	↑ (2.31) **↑ (2.57)**	-	↑ (1.91)	- **↑ (1.22)**	↑ (2.10) -	↓ (0.68)	↓ (0.76)	↓ (0.49) **↓ (0.72)**	↓ (0.59) **↓ (0.78)**

	GST				GPX				GR				G6PD			
Liver	↑ (1.26)	↑ (1.09)	↑ (1.54) **↑ (1.22)**	↑ (1.46) **↑ (1.35)**	↑ (1.41)	↑ (1.42)	↑ (1.60) **↑ (1.13)**	↑ (1.58) -	-	↓ (0.86)	↓ (0.60) **↓ (0.71)**	↓ (0.71) **↓ (0.83)**	↓ (0.74)	↓ (0.72)	↓ (0.58) -	↓ (0.75) -
Lung	↓ (0.88)	-	- -	- **↓ (0.90)**	↓ (0.59)	↓ (0.75)	↓ (0.51) -	↓ (0.76) -	-	-	↓ (0.60) **↓ (0.70)**	- **↓ (0.87)**	↓ (0.75)	↓ (0.86)	↓ (0.43) **↓ (0.57)**	- -
Kidney	↓ (0.79)	↓ (0.77)	↓ (0.67) **↓ (0.86)**	↓ (0.76) -	↓ (0.73)	↓ (0.72)	↓ (0.62) **↓ (0.85)**	↓ (0.68) -	↓ (0.66)	-	↓ (0.64) -	- -	-	-	- -	- -
Heart	-	↓ (0.78)	- -	↓ (0.64) **↓ (0.83)**	↓ (0.31)	↓ (0.61)	↓ (0.07) **↓ (0.22)**	↓ (0.13) **↓ (0.22)**	↓ (0.76)	↓ (0.72)	↓ (0.70) **↓ (0.92)**	↓ (0.56) **↓ (0.78)**	↓ (0.62)	-	↓ (0.59) -	↓ (0.67) **↓ (0.81)**
Brain	↓ (0.74)	↓ (0.78)	↓ (0.69) -	↓ (0.63) **↓ (0.81)**	↓ (0.44)	↓ (0.73)	↓ (0.24) **↓ (0.54)**	↓ (0.41) **↓ (0.56)**	↓ (0.60)	↓ (0.80)	↓ (0.52) **↓ (0.87)**	↓ (0.79) **↓ (0.86)**	-	-	↑ (1.60) **↑ (1.50)**	↓ (0.88) **↓ (0.81)**
Intestine	↓ (0.78)	-	↓ (0.73) **↓ (0.81)**	↓ (0.78) **↓ (0.87)**	↓ (0.51)	↓ (0.65)	↓ (0.36) **↓ (0.70)**	↓ (0.48) **↓ (0.15)**	↑ (1.12)	-	↑ (1.12) -	- -	-	-	↑ (1.20) **↑ (1.12)**	↓ (0.85) -
Spleen	↓ (0.60)	↓ (0.63)	↓ (0.50) -	↓ (0.62) -	↓ (0.46)	↓ (0.63)	↓ (0.38) -	↓ (0.49) **↓ (0.79)**	↓ (0.75)	↓ (0.78)	↓ (0.59) -	↓ (0.67) -	↓ (0.67)	↓ (0.87)	↓ (0.21) **↓ (0.32)**	↓ (0.81) -

FIG. 12

Organ	LOOH				TBARS				GSH				GGCS			
	+/-		-/-		+/-		-/-		+/-		-/-		+/-		-/-	
	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F
Liver	-	↑ (1.37)	-	↑ (1.13)	-	-	↓ (0.57) **↓ (0.71)**	↓ (0.69) **↓ (0.78)**	-	-	- -	- -	↑ (3.93)	-	↑ (4.45) -	↑ (1.36) **↑ (1.35)**
Lung	↑ (1.43)	↑ (1.30)	↑ (1.67) **↑ (1.27)**	↑ (2.10) **↑ (1.71)**	-	↑ (1.28)	↑ (1.25) **↑ (1.28)**	↑ (1.35) **↑ (1.39)**	-	↑ (1.07)	↑ (1.38) **↑ (1.16)**	- -	-	-	- -	- -
Kidney	↑ (1.44)	↑ (1.27)	↑ (1.43) **↑ (1.19)**	↑ (1.61) **↑ (1.36)**	-	-	- **↑ (1.11)**	↑ (1.20) **↑ (1.20)**	↑ (1.14)	↑ (1.11)	- **↑ (1.34)**	↑ (1.24) **↑ (1.27)**	↓ (0.84)	-	↓ (0.72) -	↓ (0.85) -
Heart	↑ (2.24)	↑ (2.04)	↑ (3.35) **↑ (2.28)**	↑ (2.88) **↑ (1.64)**	↑ (1.60)	↑ (1.30)	↑ (2.24) **↑ (1.78)**	↑ (1.76) **↑ (1.53)**	↑ (1.59)	↑ (1.82)	↑ (1.76) **↑ (1.14)**	↑ (2.07) **↑ (1.17)**	↓ (0.81)	↓ (0.84)	↓ (0.65) -	↓ (0.71) -
Brain	↑ (1.25)	↑ (1.30)	↑ (1.35) **↑ (1.28)**	↑ (1.47) **↑ (1.26)**	↑ (1.40)	↑ (1.29)	↑ (2.17) **↑ (1.86)**	↑ (1.84) **↑ (1.59)**	↑ (1.79)	↑ (1.44)	↑ (2.07) **↑ (1.43)**	↑ (1.57) -	-	-	- -	- **↓ (0.77)**
Intestine	↑ (1.80)	↑ (1.93)	↑ (2.46) **↑ (1.57)**	↑ (2.48) **↑ (1.60)**	↑ (1.80)	↑ (1.96)	↑ (3.39) **↑ (2.11)**	↑ (3.30) **↑ (2.09)**	↑ (2.93)	↑ (2.49)	↑ (3.02) **↑ (1.15)**	↑ (2.79) **↑ (1.13)**	↓ (0.83)	↑ (1.30)	↓ (0.71) -	↓ (0.76) -
Spleen	↑ (2.07)	↑ (2.16)	↑ (3.44) **↑ (2.10)**	↑ (3.85) **↑ (1.53)**	↑ (1.97)	↑ (1.78)	↑ (2.86) **↑ (1.96)**	↑ (2.69) **↑ (1.83)**	-	↑ (2.23)	- **↑ (1.27)**	↑ (2.47) **↑ (1.29)**	↓ (0.61)	↑ (1.40)	↓ (0.46) **↓ (0.68)**	↓ (0.79) -
	GST				GPX				GR				G6PD			
Liver	↑ (1.31)	↑ (1.57)	↑ (1.84) **↑ (1.46)**	↑ (1.66) **↑ (1.53)**	↑ (1.47)	↑ (1.63)	↑ (1.65) **↑ (1.17)**	↑ (1.80) **↑ (1.26)**	-	-	↓ (0.77) -	↓ (0.67) **↓ (0.78)**	↓ (0.78)	-	↓ (0.57) -	- **↑ (0.53)**
Lung	-	-	- -	- -	↓ (0.68)	↓ (0.80)	↓ (0.55) -	↓ (0.73) -	-	-	↓ (0.61) **↓ (0.71)**	- **↓ (0.84)**	↓ (0.77)	↑ (1.17)	↓ (0.44) **↓ (0.51)**	- **↑ (1.20)**
Kidney	↑ (1.83)	↓ (0.86)	↓ (0.77) -	- -	↓ (0.85)	-	↓ (0.78) **↓ (0.93)**	↓ (0.76) -	-	-	↓ (0.67) -	- -	-	↑ (1.23)	- **↑ (1.20)**	↑ (1.19) **↑ (1.41)**
Heart	↓ (0.21)	↓ (0.78)	- -	↓ (0.73) -	↓ (0.47)	↓ (0.74)	↓ (0.07) **↓ (0.22)**	↓ (0.17) **↓ (0.28)**	↑ (1.11)	↓ (0.73)	↓ (0.76) -	↓ (0.51) **↓ (0.71)**	-	↑ (1.16)	↓ (0.63) -	↑ (1.25) **↑ (1.50)**
Brain	↓ (0.24)	↓ (0.80)	- -	↓ (0.70) -	↓ (0.59)	↓ (0.72)	↓ (0.30) **↓ (0.69)**	↓ (0.45) **↓ (0.62)**	-	-	↓ (0.58) -	↓ (0.67) **↓ (0.84)**	↑ (1.47)	-	↑ (2.01) **↑ (1.87)**	- -
Intestine	↓ (0.38)	-	↓ (0.67) **↓ (0.86)**	- -	↓ (0.59)	↓ (0.73)	↓ (0.37) **↓ (0.71)**	↓ (0.54) -	↑ (1.20)	-	↑ (1.09) -	- -	-	-	↑ (1.22) **↑ (1.14)**	↑ (1.18) **↑ (1.25)**
Spleen	↓ (0.84)	↓ (0.69)	↓ (0.55) -	↓ (0.73) -	↓ (0.52)	↓ (0.63)	↓ (0.40) **↓ (0.88)**	↓ (0.53) **↓ (0.85)**	-	-	↓ (0.73) -	↓ (0.75) -	-	↑ (1.39)	↓ (0.23) **↓ (0.34)**	↑ (1.20) **↑ (1.38)**

FIG. 13

	DNTR	DXTR	LOOH	TBARS	G6PD	GGCS	GPX	GR	GSH	GST
Organ										
Brain			G, GD, R	GD, **G-R**	R, **G-GD**	R, **G-GD**	**GD-R**, **G-GD**	**G-GD**, **G-R**, **GD-R**	G, GD, R	G, GD
Heart	**G-GD**, **G-R**	**G-GD**, **G-R**	R, **G-GD**	G, GD, R	**THR**	**THR**	R, **G-GD**	**THR**	**G-GD**, **G-R**	G, GD, R
Intestine			GD, **G-R**	G, GD, R	GD, R	GD, **G-R**	**G-GD**, **G-R**	GD, **G-R**	G, GD, R	**THR**
Kidney			**G-GD**, **G-R**	**G-R**	GD, R	**G-GD**, **G-R**	**GD-R**, **G-GD**	**G-GD**, **G-R**		R, **G-GD**
Liver			G, GD, R	GD, **G-R**	G, **G-R**	**G-GD**	R, **G-GD**	G, GD	G, GD, R	R, **G-GD**
Lung			R, **G-GD**	G, **G-R**	R, **G-GD**		**G-GD**	**G-GD**, **G-R**	G, GD	G, GD
Spleen			**GD-R**, **G-GD**	G, GD, R	**G-GD**, G-R, **GD-R**	**THR**	G	**G-GD**, **G-R**	G, GD, R	**G-GD**, **G-R**

G → Genotype main effect
GD → Gender main effect
R→ Radiation main effect
G-GD → Genotype-Gender two way effect
G-R → Genotype-Radiation two way effect
GD-R → Gender-Radiation two way effect
THR → Three way effect (Gender-Genotype-Radiation)